DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

February 13, 2015

LIN-ZHI INTERNATIONAL, INC.
BERNICE LIN, PH.D.
VP OF OPERATIONS
670 ALMANOR AVE
SUNNYVALE CA 94085

Re: K141205
Trade/Device Name: LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay
LZI Oral Fluid 6-Acetylmorphine Calibrators
LZI Oral Fluid 6-Acetylmorphine Controls
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate test system
Regulatory Class: II
Product Code: DJG, DKB, DIF
Dated: February 2, 2015
Received: February 4, 2015

Dear Dr. Bernice Lin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

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For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k141205

Device Name
LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay
LZI Oral Fluid 6-Acetylmorphine Calibrators
LZI Oral Fluid 6-Acetylmorphine Controls

Indications for Use *(Describe)*

The LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of 6-Acetylmorphine in neat human oral fluid, collected into the LZI Oral Fluid Collector, at the cutoff value of 4 ng/mL. The assay is designed for prescription use with a number of automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as GCMS and LCMS or (2) permitting laboratories to establish quality control procedures.

The LZI Oral Fluid 6-Acetylmorphine Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay at the cutoff value of 4 ng/mL.

The LZI Oral Fluid 6-Acetylmorphine Controls are for use as assayed quality control materials to monitor the precision of the LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay at the cutoff value of 4 ng/mL.

The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Introduction

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter name, Address, and Contact

Lin-Zhi International, Inc.
670 Almanor Avenue
Sunnyvale, CA 94085
Phone: (408) 732-3856
Fax: (408) 732-3849
e-mail: bclin@lin-zhi.com

Contact: Bernice Lin, Ph.D.
VP Operations

Preparation Date

February 12, 2015

Device Name and Classification

Classification Name:	Enzyme Immunoassay, Opiates Class II, DJG (91 Toxicology), 21 CFR 862.3650
	Drug Specific Calibrators, Class II, DLJ (91 Toxicology), 21 CFR 862.3200
	Drug Specific Controls, Class I, LAS (91 Toxicology), 21 CFR 862.3280
Common Name:	Homogeneous Oral Fluid 6-Acetylmorphine Enzyme Immunoassay
Proprietary Name:	LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay, LZI Oral Fluid 6-Acetylmorphine Calibrators LZI Oral Fluid 6-Acetylmorphine Controls

Legally Marketed Predicate Device(s)

The LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay (EIA) (k141205) is substantially equivalent to the Lin-Zhi International, Inc. 6-Acetylmorphine Enzyme Immunoassay, Calibrators and Controls for Hitachi 717 Systems (k101195) manufactured by Lin-Zhi International, Inc. The LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay is identical or similar to its predicate in terms of intended use, method principle, device components, and clinical performance.

Device Description

The LZI Oral Fluid 6-Acetylmorphine assay is a homogeneous enzyme immunoassay with ready-to-use liquid reagent. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the drug concentration in the sample is measured in terms of enzyme activity. In the absence of drug in the sample, 6-Acetylmorphine-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when free drug is present in the sample, antibody would bind to free drug, the unbound 6-Acetylmorphine-labeled G6PDH then exhibits its maximal enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that can be measured spectrophotometrically at 340 nm.

The LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay is a kit comprised of two reagents, an R_1 and R_2 which are bottled separately but sold together within the kit.

The R_1 solution contains mouse monoclonal anti-6-Acetylmorphine antibody, glucose-6-phosphate (G6P) nicotinamide adenine dinucleotide (NAD), stabilizers, and sodium azide (0.09%) as a preservative. The R_2 solution contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with 6-Acetylmorphine in buffer with sodium azide (0.09%) as preservative.

The LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay calibrators and controls designated for use at the 4 ng/mL cutoffs contain 0, 2, 4, 6, 10, and 20 ng/mL of 6-Acetylmorphine in synthetic oral fluid matrix with sodium azide (0.09%) as preservative. These five calibrators and two controls are sold as individual bottles.

Intended Use

The LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of 6-Acetylmorphine in neat human oral fluid, collected into the LZI Oral Fluid Collector, at the cutoff value of 4 ng/mL. The assay is designed for prescription use with a number of automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as GC/MS or (2) permitting laboratories to establish quality control procedures.

The LZI Oral Fluid 6-Acetylmorphine Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay at the cutoff value of 4 ng/mL.

The LZI Oral Fluid 6-Acetylmorphine Controls are for use as assayed quality control materials to monitor the precision of the LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay at the cutoff value of 4 ng/mL.

The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

Comparison to Predicate Device

The LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay (k141205) is substantially equivalent to the Lin-Zhi International, Inc. 6-Acetylmorphine Enzyme Immunoassay, Calibrators and Controls for Hitachi 717 Systems cleared by the FDA under the premarket notification k101195 for its stated intended use.

The following table compares LZI's Oral Fluid 6-Acetylmorphine Enzyme Immunoassay with the predicate device.

Device Characteristics	**Subject Device (k141205)** LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay, Calibrators and Controls	**Predicate Device (k101195)** LZI 6-Acetylmorphine Enzyme Immunoassay, Calibrators and Controls
Intended Use	The LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay, when used in conjunction with the Beckman AU400e automated clinical system analyzers, is intended for the qualitative and semi-quantitative determination of 6-Acetylmorphine in neat human oral fluid, collected into the LZI Oral Fluid Collector, at the cutoff value 4 ng/mL. The assay is designed for prescription use with a number of automated clinical chemistry analyzers. ***This assay provides a rapid screening procedure for determining the presence of 6-Acetylmorphine in oral fluid. The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.***	The LZI 6-Acetylmorphine Enzyme Immunoassay, when used in conjunction with Hitachi 717 automated clinical system analyzers, is intended for the qualitative and semi-quantitative determination of 6-Acetylmorphine in human urine, at a cutoff value of 10 ng/mL. The assay is designed for professional use with a number of automated clinical chemistry analyzers. ***This assay provides a rapid screening procedure for determining the presence of 6-Acetylmorphine in urine. The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.***
Analyte	6-Acetylmorphine	6-Acetylmorphine
Cutoff	4 ng/ml	10 ng/mL
Matrix	Oral fluid	Urine
Calibrator Levels	5 Levels (0, 2, 4, 10, 20 ng/mL)	5 Levels (0, 5, 10, 20, 40 ng/mL)
Control Levels	2 Levels (2 ng/mL, 6 ng/mL)	2 Levels (7.5 ng/mL, 12.5 ng/mL)
Storage	2-8 ºC until expiration date	2-8 ºC until expiration date

Performance Characteristics Summary:

Beckman AU400e Analyzer

Precision:

Semi-Quantitative Positive/Negative Results:

4 ng/mL Cutoff Result:		Total Precision		Within Run Precision	
Sample Concentration	**% of Cutoff**	**Number of Determination**	**Immunoassay Result**	**Number of Determination**	**Immunoassay Result**
0 ng/mL	-100.0%	80	80 Negative	20	20 Negative
1 ng/mL	-75.0%	80	80 Negative	20	20 Negative
2 ng/mL	-50.0%	80	80 Negative	20	20 Negative
3 ng/mL	-25.0%	80	80 Negative	20	20 Negative
4 ng/mL	100.0%	80	32 Pos/48 Neg	20	8 Pos/12 Neg
5 ng/mL	+25.0%	80	80 Positive	20	20 Positive
6 ng/mL	+50.0%	80	80 Positive	20	20 Positive
7 ng/mL	+75.0%	80	80 Positive	20	20 Positive
8 ng/mL	+100.0%	80	80 Positive	20	20 Positive

Qualitative (ΔOD Value) Positive/Negative Results:

4 ng/mL Cutoff Result:		Total Precision		Within Run Precision	
Sample Concentration	**% of Cutoff**	**Number of Determination**	**Immunoassay Result**	**Number of Determination**	**Immunoassay Result**
0 ng/mL	-100.0%	80	80 Negative	20	20 Negative
1 ng/mL	-75.0%	80	80 Negative	20	20 Negative
2 ng/mL	-50.0%	80	80 Negative	20	20 Negative
3 ng/mL	-25.0%	80	80 Negative	20	20 Negative
4 ng/mL	100.0%	80	18 Pos/62 Neg	20	4 Pos/16 Neg
5 ng/mL	+25.0%	80	80 Positive	20	20 Positive
6 ng/mL	+50.0%	80	80 Positive	20	20 Positive
7 ng/mL	+75.0%	80	80 Positive	20	20 Positive
8 ng/mL	+100.0%	80	80 Positive	20	20 Positive

Analytical Recovery:

Expected Value (ng/mL)	Observed Value (ng/mL)	% Recovery
1	1.2	120.0
2	2.2	110.0
4	4.3	107.5
6	5.8	96.7
8	8.1	101.3
10	10.1	101.0
12	12.1	100.8
14	15.0	107.1
16	16.8	105.0
18	18.8	104.4
20	20.6	103.0

Method Comparison: Clinical Samples

From a total of one-hundred-fifty (150) clinical unaltered samples

Clinical Samples Correlation Results: Semi-Quantitative Accuracy Study

Discrepant samples determined as compared to the Estimated GC/MS Total Value

4 ng/mL Cutoff	**Negative**	**< 50 % of the cutoff** concentration by GC/MS analysis	**Near Cutoff Negative** (Between 50 % below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50 % above the cutoff concentration)	**High Positive** (Greater than 50 % above the cutoff concentration)	**% Agreement**
Positive	0	0	0	10	89	99.0%
Negative	20	14	16	1*	0	100.0%

Discrepant Sample #	**GC/MS 6AM (ng/mL)**	**Pos/ Neg Result**	**AU400e Immunoassay Semi-Quantitative Result (ng/mL)**	**Pos/ Neg Result**
51*	4.2	+	3.5	-

Clinical Samples Correlation Results: Qualitative Accuracy Study (ΔOD, mAu)

4 ng/mL Cutoff	**Negative**	**< 50 % of the cutoff** concentration by GC/MS analysis	**Near Cutoff Negative** (Between 50 % below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50 % above the cutoff concentration)	**High Positive** (Greater than 50 % above the cutoff concentration)	**% Agreement**
Positive	0	0	0	9	89	98.0%
Negative	20	14	16	2*	0	100.0%

Discrepant Sample #	**GC/MS 6AM (ng/mL)**	**Pos/ Neg Result**	**AU400e Immunoassay Qualitative Result (mAu)**	**Cutoff ΔOD (mAu)**	**Pos/ Neg Result**
51*	4.2	+	662.9	678.6	-
52*	4.4	+	675.3	701.6	-

Endogenous Compound Interference and Specificity - Cross-Reactivity:

No significant undesired cross reactants or endogenous substance interference was observed at physiologically relevant concentrations. Ascorbic Acid concentrations above 3 mg/mL cause false-negative results. See product insert for list of compounds tested.

Shipping/Recovery Stability Study:

No significant sample degradation occurred following real-time and accelerated stability studies up to 72 hours. All sample shipments are based on the assumption of a 24 hour priority overnight delivery.

Sample Storage Stability Study:

No significant sample degradation occurred following real-time stability studies. Based on real-time studies, samples can be stored at 2-8 ºC for up to 15 Days. Based on real-time studies, samples can be stored at -20 ºC for up to 113 Days. Real-time stability studies are on-going.

Open (and re-capped) vial Stability for Reagent and Calibrator/Control:

Real time (2-8ºC) and accelerated stability studies (at room temperature, ~25ºC and 30ºC) were performed. Results indicated that opened and recapped calibrators and controls are stable for 6 months when stored at (2-8ºC).

Closed vial Stability for Calibrator/Control:

Real time (2-8ºC) stability studies were performed. Results indicated that unopened calibrators and controls are stable for 6 months when stored at 2-8ºC.

Summary:

The information provided in this pre-market notification demonstrates that the LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay is substantially equivalent to the legally marketed predicate device for its general intended use. Substantial equivalence was demonstrated through comparison of intended use and physical properties to the commercially available predicate device as confirmed by gas chromatography/mass spectrometry (GC/MS), an independent analytical method. The information supplied in this pre-market notification provides reasonable assurance that the LZI Oral Fluid 6-Acetylmorphine Enzyme Immunoassay is safe and effective for its stated intended use.